REMARKS

Claims 1-12 and 15-18 are in this application. Claims 13 and 14 have been cancelled and claims 15-18 have been added.

Claim 1 has been amended to define PVC as polyvinylchloride, EVA as ethylene-vinyl acetate and PET as polyvinylchloride. Support for the amendment of claim 1 to replace the term "container" with "well" is based on the description of a microtiter plate. Attached are references from Wikipedia and NationMaster.com that describe microtiter plates as flat plates with multiple wells.

Claim 3 has been amended to define PVDF as polyvinylidene fluoride.

Claim 8 was amended to include the phrase "bovine spongiform encephalopathy". The use of TSE in claim 12 was a typographical error. The correct abbreviation is "BSE".

In claim 10 the word "bar" was a typographical error. The correct word was "by".

New claims 15 and 16 have been added. Support for these claims is found in the previous version of claim 2. New claim 17 has been added. Support for this claim is found in the previous version of claim 10. New claim 18 has been added. Support for this claim is found in the previous version of claim 12.

The Examiner has rejected claims 13 and 14 under 35 USC 101 as being nonstatutory. The use of the microtiter plate is defined in the method claims 10-12, 17 and 18. Therefore, Claims 13 and 14 have been cancelled.

The Examiner has rejected claims 1-14 under 35 USC 103(a) as being unpatentable over Glezer et al. in view of Coleman et al. This is respectfully traversed.

The present invention relates to a microtiter plate and a method for the detection of analytes in a sampling using the microtiter plate which enables the simultaneous detection of multiple analytes in a sample.

Claim 1 includes:

1. a microtiter plate;

2. comprising a plurality of containers of a rigid material selected from the group consisting of glass, polystyrene, polyacryl, polyamide, polyethylene, polypropylene, acrylate, butadiene , styrene (ABS), Barnox, PVC, nylon, EVA, PET and combinations thereof, wherein each container is a well of a regular microtiter plate,

3. the bottom of each container is comprised of a (semi-) permeable membrane filter,

4. the filter is capable of directly or indirectly binding an analyte,

5. each well is separated from an adjacent well by a well dividing wall,

6. the wells are grouped in one or more clusters, each cluster comprising at least two wells, 7. the clusters are separated from adjacent clusters by a cluster dividing wall, and

8a. at least part of the container dividing wall is lower than the cluster dividing wall or

8b. the well dividing wall contains at least one passageway connecting at least two adjacent wells within a cluster, and the passageway is at a distance from the bottom of the well and at least partly below the top of the well.

Glezer discloses a method for conducting multiple chemical, biochemical and/or biological assays on a sample. The method involves the use of a Multi-Domain Multi- Well Plate or MDMW Plate comprising a plurality of wells, each comprising a plurality of assay domains.

It is essential to note that Glezer discloses in §[0006] of page 1:

"assay modules having one or more assay cells (e.g. wells, compartments, chambers, channels, flow cells, etc.) that comprise a plurality of assay domains[....]; the plates comprising a plurality of wells, one or more of the wells comprising a plurality of assay domains (referred to herein as Multi-Domain Multi-Well Plates or MDMW Plates) see § [0006] on page 1).

Thus, the assay modules (MDMW plates) of Glezer comprise a plurality of assay cells (wells) that comprise a plurality of assay domains (the fluid containment regions).

It follows that a fluid containment region as defined in Glezer is not an assay cell (well), whereas the present claim requires that the container is a well of a regular microtiter plate. Hence, Glezer does not disclose the claimed plate.

In addition, Glezer does not have the feature that the bottom of each container is comprised of a (semi-) permeable membrane filter.

The difference between the presently claimed invention and the plate described in Glezer is that the containers grouped in clusters in the present invention are the wells of a microtiter plate, whereas in Glezer the "containers" grouped in clusters are the assay domains formed by holes in a dielectric layer applied on top of an electrode in the bottom of the well.

In the claimed invention a much simpler configuration is obtained. This is best illustrated by the phrasing on page 19, lines 29 - page 20, line 4, of the description of the present application which states that:

In order to produce a microtiter plate that is particularly useful for distinctly detecting multiple analytes in one sample according to a method of the invention, the skilled person will understand that the walls of adjacent containers in a standard microtiter plate may be reduced in height or (partially) removed by milling away (part of) the walls separating two or more adjacent containers.

and the phrasing on page 16, lines 16-20, which states that:

In an alternative embodiment of a microtiter plate according to the present invention, the container walls and cluster walls need not differ in height but, instead, a passageway, for instance in the form of an indent or opening, bore or gate, is provided between individual containers within a cluster, but not between individual containers between clusters.

Thus, the microtiter plate of the present invention is based on a standard microtiter plate. In contrast, the electrodes in a plate of Glezer are patterned, using for instance such techniques as photolithographic techniques (e.g. established techniques in the microfabrication of electronics) (paragraph [0100] of Glezer). The dielectric layer is also deposited in patterns, for instance through the use of established photolithographic techniques (e.g., techniques used in the semiconductor electronics industry) (paragraph [0114] of Glezer 1). This is not a simple process and will not provide the product claimed in this application.

Another advantage of the claimed invention is that in the claimed method the claimed microtiter plate is used. It can be filled using standard fluid delivery systems for microtiter plates.

It is clear that Glezer does not provide for such a plate, since in Example 9 it is indicated that microdispensing techniques must be used for the deposition of analytes to the four isolated "fluid containment regions" on the working electrode surface within each well of Fig. 10C, so that the standard fluid delivery systems for microtiter plates cannot be used.

On page 15, § [0112], Glezer discloses that the electrodes may be porous. But included in Glezer in § [0084] on page 11 is the following disclosure:

> According to another embodiment, the first electrode surface (e.g., working electrode surface) is centered at the bottom of each well and the second electrode surface (e.g. counter electrode surface) is adjacent the periphery of the bottom of each well. In some embodiments, the working electrode surface is centered at the bottom of each well and is completely surrounded by the counter electrode surface.

This concurs with the disclosure in Figures 10B, 10C and 10D, wherein the electrode forms only a portion of the bottom.

In fact in §[0085] on page 11 it is stated that:

> "the working electrode surfaces are small, e.g., relative to the surface area of a well or well bottom".

and that

> "The multi-well assay module has a plurality of wells, each well having a well bottom comprising a first electrode surface, a second electrode surface and a dielectric surface

(preferably the dielectric surface is the surface of the bottom of the well between the first electrode surface and the second electrode surface), wherein the ratio of the first electrode surface and the dielectric surface (or alternatively the surface of the well bottom) is less than 1 to 5, preferably 1 to 10, more preferably 1 to 30".

Thus, the electrode, if present, and if porous, forms only a part of the bottom of each well. Glezer does not disclose a multiwell plate wherein a membrane is used as a plate bottom.

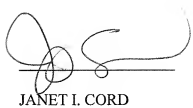
In summary, Glezer does not disclose nor suggest many of the features of the claimed invention including the bottom of each container is comprised of a (semi-) permeable membrane filter.

The disclosure of Coleman with Glezer does not teach nor suggest the reference. The structure of Coleman so differs from Glezer and the claimed invention that it does not suggest the claimed invention. For example, it is clear from the description in column 3, lines 10-25 and description of Figures 1 and 2 in column 5, lines 30-59, of Coleman that the configuration so differs from the claimed invention, that the combination of references does not teach or suggest the claimed invention.

Therefore, as none of the claims are obvious, it is respectfully requested that the rejection be withdrawn.

It is submitted that the application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted,



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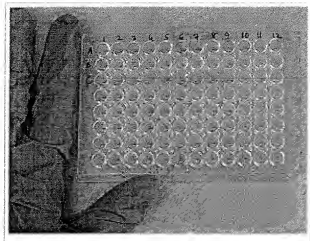
Microtiter plate

From Wikipedia, the free encyclopedia

A **Microtiter plate** (spelt Microtitre in Europe) or **microplate** is a flat plate with multiple "wells" used as small test tubes. The microplate has become a standard tool in analytical research and clinical diagnostic testing laboratories. A very common usage is in the enzyme-linked immunosorbent assay (ELISA), the basis of most modern medical diagnostic testing in humans and animals.



A 96-well microtiter plate. This plate could be used for ELISA.

A microplate typically has 6, 24, 96, 384 or even 1536 sample wells arranged in a 2:3 rectangular matrix. Some microplates have even been manufactured with 3456 or even 9600 wells, and an "array tape" product has been developed that provides a continuous strip of microplates embossed on a flexible plastic tape.[1]

Each well of a microplate typically holds somewhere between tens of nanolitres to several millilitres of liquid. They can also be used to store dry powder or as racks to support glass tube inserts. Wells can be either circular or square. For compound storage applications, square wells with close fitting silicone cap-mats are preferred. Microplates can be stored at low temperatures for long periods, may be heated to increase the rate of solvent evaporation from their wells and can even be heat-sealed with foil or clear film. Microplates with an embedded layer of filter material were developed in the early 1990s by several companies, and in 1992, the world's first Solid Phase Extraction (SPE) microplate was launched by Porvair Sciences. This allowed simple column chromatography to be carried out in a microplate footprint for the first time. Today there are microplates for just about every application in life Science research which involves filtration, separation, optical detection, storage, reaction mixing or cell culture.

The enormous growth in studies of whole live cells has led to an entirely new range of microplate products which are "tissue culture treated" especially for this work. The surface of these products is modified, using a plasma discharge, to make it easier for adherent cells to grow on.

A number of companies have developed robots to specifically handle SBS microplates. These robots may be liquid handlers which aspirate or dispense liquid samples from and to these plates, or "plate movers" which transport them between instruments, plate stackers which store microplates during these processes, plate hotels for longer term storage or microplate incubators to ensure constant temperature during testing.

Instrument companies have designed plate readers which can detect specific biological, chemical or physical events in samples stored in these plates.

Contents

Manufacture and composition

Microplates are manufactured in a variety of materials. The most common is polystyrene, used for most optical detection microplates. It can be coloured white by the addition of titanium dioxide for optical absorbance or luminescence detection or black by the addition of carbon for fluorescent biological assays. Polypropylene is used for the construction of plates subject to wide changes in temperature, such as storage at -80C and thermal cycling. It has excellent properties for the long-term storage of novel chemical compounds. Polycarbonate is cheap and easy to mould and has been used for disposable microplates for the polymerase chain reaction (PCR) method of DNA amplification. Cyclo-olefins are now being used to provide microplates which transmit ultraviolet light for use in newly developed assays.

The most common manufacturing process is injection moulding, used for polystyrene, polypropylene and cyclo-olefin. Vacuum forming can be used with softer plastics such as polycarbonate. Composite microplates, such as filter plates and SPE plates and even some advanced PCR plate designs use multiple components which are moulded separately and later assembled into a finished product. ELISA plates may now be assembled from twelve separate strips of eight wells, making it easier to only partially use a plate. This saves cost for the scientist.

History

The earliest microplate was created in 1951 by a Hungarian, Dr. G. Takatsky, who machined 6 rows of 12 "wells" in Lucite. However, common usage of the microplate began in the late 1950s when John Liner in USA had introduced a molded version. By 1990 there were more than 15 companies producing a wide range of microplates with different features. It was estimated that 125 million microplates were used in 2000 alone. The word "Microtiter" is a trademark registered by the Dynatech company; it is now more usual to use the generic term "microplate".

In 1996, the Society for Biomolecular Screening (SBS) began an initiative to create a standard definition of a microtiter plate. A series of standards was proposed in 2003 and published by the American National Standards Institute (ANSI) on behalf of the SBS. The standards govern various characteristics of a microplate including well dimensions (e.g. diameter, spacing and depth) as well as plate properties (e.g. dimensions and rigidity).

References

1. ^ Elaine May (2007-06-15). "Array Tape for Miniaturized Genotyping (http://www.genengnews.com/articles/chtitem.aspx?tid=2136)", *Genetic Engineering & Biotechnology News*, Mary Ann Liebert, Inc., p. 22. Retrieved on 6 July 2008. "(subtitle) Processing hundreds of microplate equivalents without complex plate-handling equipment"

External links

- Microplate History 2nd Edition May 1999 by Roy Mann (http://www.microplate.org/history/det_hist.htm)
- Society for Biomolecular Screening (http://www.sbsonline.org/)
- A sample image of some 96-well microtiter plates (http://www.freewebs.com/immunology/microtiter-plates.html)
- American National Standards Institute (http://www.ansi.org/)
- Chemical Compatibility of various microplate materials and filters (http://www.porvair-sciences.com/docs/Porvair_compatibility_nomenu.pdf)
- The effect of plasticizers on sample integrity in polypropylene microplates (http://www.porvair-sciences.com/docs/Extract.pdf)
- European Laboratory Robotics Interest Group - specialisuing in automation of microplate processes (http://www.elrig.org/)
- Microplate application notes for Life Science research (http://www.porvair-sciences.com/reply.htm)

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Category: Laboratory equipment

Encyclopedia > Microtiter plate

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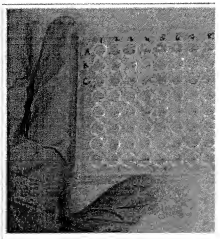

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External links

- Microplate History 2nd Edition May 1999 by Roy Mann
- Society for Biomolecular Screening
- A sample image of some 96-well microtiter plates
- American National Standards Institute
- Glass Microtiter Plates

Laboratory equipment

Agar plate | Aspirator | Bunsen burner | Calorimeter | Colony counte Colorimeter | Centrifuge | Fume hood | Magnetic stirrer | Microscope **Microtiter plate** | Plate reader | Spectrophotometer | Stir bar | Thermometer | Vortex mixer | Static mixer

Laboratory glassware

Beaker | Boiling tube | Büchner funnel | Burette | Conical measure Crucible | Cuvette | Laboratory flasks (Erlenmeyer flask, Round-bottc flask, Florence flask, Volumetric flask, Büchner flask, Retort) | Gas syri | Graduated cylinder | Pipette | Petri dish | Separating funnel | Soxhl extractor | Test tube | Thistle tube | Watch glass

Categories: Chemistry stubs | Laboratory equipment

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